CASE STUDY

Case Study: Management Decisions in a Comorbid Patient With Type 2 Diabetes Having Primary Hyperlipidemia

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Key Point: Type 2 diabetes mellitus (T2DM) and primary hyperlipidemia are risk factors for cardiovascular disease (CVD) that warrant timely management of both disorders. An option for treating T2DM is Welchol® (colesevelam HCl), which represents an effective and safe way to treat patients with elevated glycosylated hemoglobin (A1C) and low-density lipoprotein cholesterol (LDL-C).

Background

Nancy is a 60-year-old Caucasian woman who works in a corporate office. She has a sedentary job as an administrative assistant. Nancy has two grown children; her elderly mother moved in 3 months ago, and Nancy is now responsible for her care. Nancy is concerned about having to pay for extra medical expenses as her husband recently lost his job. Nancy has not seen her primary care physician (PCP) recently, but now goes for a 6-month follow-up visit. Her PCP had previously started Nancy on lifestyle modification (diet and exercise), metformin, and simvastatin.

Current Visit

Physical Exam

- Weight 175 lb
- Height 5 ft 4 in
- Body Mass Index (BMI) 30
- Blood Pressure 125/80 mmHg

Current Treatment Regimen

- Metformin 850 mg daily
- Simvastatin 40 mg daily
- Aspirin 81 mg daily

Health History

- Hyperlipidemia diagnosed 1 year ago
- T2DM diagnosed 1 year ago
- Former smoker (quit 2 years ago; was a 1 pack/day cigarette smoker)
- Diet: Reports that she tries to limit fat intake, has decreased consumption of high-sugar sweets to twice a week, and has wine with dinner on weekends
- Limited exercise mainly on weekends and walks associated with shopping
- Family history: Her mother has a history of CVD; her father, diagnosed with T2DM, died of a heart attack at 65 years of age

Laboratory Results

Laboratory Tests	Current Visit	Previous Visit
A1C	7.5%	7.30%
Fasting Blood Glucose (FBG)	135 mg/dL	120 mg/dL
LDL-C	118 mmol/L	180 mmol/L
High-density lipoprotein (HDL)	47 mg/dL	49 mg/dL
Fasting triglyceride levels	182 mg/dL	205 mg/dL

Clinical Discussion

Clearly, Nancy's metabolic risk has not improved enough since her last visit to her PCP. The American College of Cardiology Foundation (ACCF) and the American Diabetes Association (ADA) Consensus Statement states that a patient classified as having T2DM has a high risk for CVD: the stated goal is LDL <100 mg/dL, and a patient having at least one risk factor is at highest risk for CVD and has a stated goal LDL<70 mg/dL.[1] Nancy's A1C level has increased to 7.5% despite starting on metformin; the ADA and the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) have recommended goals for A1C as <7% and ≤6.5%, respectively; both societies recommend goals for A1C as close to normal as possible (defined as A1C<6% provided no comorbidities). Nancy's lipid levels have improved, but are still too high at 118 mg/dL.[2] Her HDL cholesterol level is 47 mg/dL, and her fasting triglycerides are 182 mg/dL. She is obese with a BMI of 30.0; her FBG level increased to 135 mg/dL. Nancy's PCP increases her metformin to 1000 mg twice a day, and her simvastatin to 80 mg/d.

Three Months Later

Three months later on this regimen, Nancy's A1C level is at 7.1%, her LDL-C is now at 108 mmol/L, and her triglycerides are at 180 mg/dL. Nancy's current weight is 165 pounds, and her BMI has gone down to 28.3. Given the fact that her glucose and lipid levels are still not at goal, a consultation with an endocrinologist is made.

Endocrinologist Consultation

The endocrinologist considers how to intensify Nancy's treatment as she is not at goal for her lipid and glucose levels. Nancy is already at the upper limit of the recommended dosage for simvastatin, so going beyond 80 mg is not an option; neither is increasing the dose of metformin. Nancy would like to keep the cost of any new medications to a minimum. The endocrinologist considers adding glimepiride, which would be cost effective. However, with an A1C of 7.1%, she is at risk for hypoglycemia. Adding a dipeptidyl peptidase IV (DPP-IV) inhibitor and Zetia® (ezetimibe) could help improve both glucose and LDL levels with low risk of hypoglycemia; however, it would require two expensive co-pays imposed by her health plan to obtain these branded medications. The endocrinologist reviews the risk benefit ratio of these agents, with minimal potential of inducing hypoglycemia and liver effect, with Nancy. However, Nancy tells him that she cannot pay for two brand medications. After further consideration, the endocrinologist recommends that Nancy consider taking one drug that would reduce both her glucose and lipid levels. He explains about Welchol® (colesevelam HCl) that reduces both A1C and LDL-C, and in clinical studies there was no significant increase in body weight. He explains to Nancy that Welchol® will lower both her LDL-C and her A1C without being systemically absorbed, and she will only have to pay one branded co-pay. Nancy was given the choice of the two approved Welchol® formulations, 6 tablets that she can take all at once, or as 3 tablets twice daily, or she can take the once daily Welchol® for oral suspension, which is mixed with 4-8 oz of water.

There are several good reasons in Nancy's case for prescribing Welchol®. Her hyperglycemia and hyperlipidemia are still not under control after 1 year of therapy. She is concerned about controlling her CVD risk, but she is worried about accruing more co-pays than is necessary. She is pleased to hear that the safety of Welchol® has been established through an extensive clinical trial program; for more than 9 years, it has been an approved treatment option for patients with high LDL-C levels, and it is available in a formulation for oral suspension. Nancy's endocrinologist informs her PCP of the change he has made and returns her to his care for follow-up and long-term management.

Three Months After the Endocrinology Consultation

Three months later, Nancy's laboratory values show she is now closer to goal (see testing results below), and therapy will continue.

- LDL-C 91 mmol/L
- Triglycerides 192 mg/dL
- A1C 6.6%

Comment

Risk factors for T2DM and CVD often cluster and include obesity, insulin resistance, hyperglycemia, dyslipidemia, and hypertension.[1] The ACE/AACE consensus statement and the ADA/European Association for the Study of Diabetes guidelines agree that intervention should be early, intensive, and stringently focused on maintaining glycemic levels as close as possible to the nondiabetic range (A1C<6.0%) without causing side effects.[2,3] Setting individual goals for A1C levels in patients is dependent on a number of factors, including family history, presenting symptoms, age, comorbidities, and duration of disease.[1] A consensus statement from the ADA and the ACCF recommends treatment goals for lipid levels in patients with cardiometabolic risk (CMR).[1] (see **Table**)

TABLE. Suggested Treatment Goals in Patients With CMR and Lipoprotein Abnormalities[1]

	Goals		
	LDL cholesterol (mg/dl)	Non-HDL cholesterol (mg/dl)	ApoB (mg/dl)
Highest-risk patients, including those with 1) known CVD or 2) diabetes plus one or more additional major CVD risk factor	<70	<100	<80
High-risk patients, including those with 1) no diabetes or known clinical CVD but two or more additional major CVD risk factors or 2) diabetes but no other major CVD risk factors	<100	<130	<90

Other major risk factors (beyond dyslipoproteinemia) include smoking, hypertension, and family history of premature CAD.
CMR=cardiometabolic risk; CVD=cardiovascular disease; ApoB=Apolipoprotein B; CAD=coronary artery disease.
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New Treatment Regimen With Add-On Therapy

Welchol® is indicated as an adjunct to diet and exercise to reduce elevated LDL-C in patients with primary hyperlipidemia as monotherapy, or in combination with a statin. Welchol® is also indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.[4] Welchol® has been used as an oral tablet since its approval in 2000. The most recent formulation, and the one prescribed for Nancy, is the powder for oral suspension taken once a day with 4-8 oz of water. Adverse events reported in ≥2% of patients in clinical trials with Welchol® were constipation, nasopharyngitis, dyspepsia, hypoglycemia, nausea, and hypertension. Welchol® is not systemically absorbed and is the only agent currently approved by the US Food and Drug Administration for treating hyperlipidemia and hyperglycemia in adult patients with T2DM, regardless of their background treatment.

The safety and efficacy of Welchol® in reducing A1C and LDL-C levels have been demonstrated in clinical trials in combination with a sulfonylurea, metformin, and insulin.[5-7] Patients in the metformin study had significant reductions in A1C (-0.54%; p<0.001). Welchol® also reduced mean LDL-C and highly-sensitive C-reactive protein (hs-CRP). TG levels should be monitored for potential increase.

Treatment Goals for Nancy

- Continue lower calorie diet for further weight loss
- Increased physical activity
- Consultation with her diabetes educator on a regular basis

Conclusion

Welchol® is a safe and effective add-on therapy to metformin and simvastatin, when A1C and LDL-C levels are not at recommended goals.

Please see adjacent pages for Important Safety Information and Brief Summary of Full Prescribing Information about Welchol.

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